Superficial Radiation Therapy for the Treatment of Nonmelanoma Skin Cancers

[a]SEAN McGREGOR, DO, PHARMD; JOHN MINNI, DO, FAOCD; DAVID HEROLD, MD, MBA

[a]Broward Health Medical Center, Fort Lauderdale, Florida; [b]Waters Edge Dermatology, Port Saint Lucie, Florida; [c]Waters Edge Dermatology, Palm Beach Gardens, Florida

ABSTRACT

Superficial radiation therapy has become more widely available to dermatologists. With the advent of more portable machines, it has become more convenient for dermatology practices to employ in an office-based setting. The goal of this paper is to provide a deeper insight into the role of superficial radiation therapy in dermatology practice and to review the current literature surrounding its use in the treatment of both basal and squamous cell carcinomas.
(*J Clin Aesthet Dermatol.* 2015;8(12):12–14.)

Basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), collectively known as nonmelanoma skin cancer(s) (NMSC), are the most frequently observed malignancies in the Caucasian population.[1] A national survey in Australia estimated that approximately 75 percent of all NMSCs are BCC, with the remaining 25 percent being SCC.[2] These estimates transcend across all individuals of a fair skin type, and represent a significant healthcare burden, not only in relation to morbidity and mortality, but also healthcare costs as well.[1] Likewise, there are numerous treatment options available for the treatment of NMSC. Procedural-based options include: standard excision, curettage, curettage with electrodessication, and Mohs micrographic surgery (MMS), with MMS being the gold standard for the definitive treatment of NMSC. Topical therapies, such as imiquimod and 5-fluorouracil cream, have been used effectively in the treatment of low-risk NMSC and superficial BCC, respectively. Additionally, vismodegib, a selective inhibitor of hedgehog pathway activation, is an oral medication approved for use in metastatic and locally advanced BCC.[1] Radiation therapy is another viable option that has been used for the treatment of NMSC since the 1900s.[3] The use of radiation therapy declined since the development of MMS. However, with advances in radiation technology, we have seen a resurgence in the use of radiation therapy, more specifically, superficial radiation therapy (SRT) in the treatment of NMSC. In dermatology practice, radiation therapy is primarily used in the treatment of both BCC and SCC, both definitively and as adjunctive therapy. The primary goal of this article is to review the current literature surrounding the use of superficial radiation therapy in the treatment of NMSC and to provide insight regarding patient selection.

Any discussion regarding radiation therapy would be incomplete without proper definition of the terminology utilized in radiation oncology. Dosing is based on the International Unit known as a Gray (Gy), which is equivalent to 100cGy, and the dose delivered during one treatment session is known as a fraction.[4] For example, a typical dosing schedule for SRT might be a total dose of 4,500cGY delivered in 300cGy doses for a total of 15 fractions.[4] This dosing scheduled may be delivered over a three-week period with fractions given Monday through Friday. However, alternate dosing schedules are also used in clinical practice, which include 2 to 3 fractions per week (i.e., Monday, Wednesday, Friday schedule). Additionally, dosing of SRT is based on both the size of the tumor and the age of the patient, and radiation physicists play a key role in the determination of such doses. A number of dosing schedules are shown in Table 1 for further clarification.

SRT utilizes X-Rays, or photons, to deliver electromagnetic energy to rapidly dividing cells in order to effectively stop mitosis.[4] SRT machines deliver low energy kilovoltage photons in the range of 50 to 150kVp.[4] This is in stark contrast to the traditional machines used in radiation oncology, which deliver high-energy megavoltage photons in the range of 6 to 25mV through the use of a linear accelerator (LINAC).[4] Furthermore, there are dramatic differences in the depth of tissue penetration between

DISCLOSURE: The authors report no relevant conflicts of interest.
ADDRESS CORRESPONDENCE TO: Sean McGregor, DO, PharmD; E-mail: seanmcgr@pcom.edu

TABLE 1. Example of superficial radiation therapy dose fractionation schedules[4]

DOSE FRACTIONATION SCHEDULE (TOTAL)	INDICATION(S)
500cGy/fraction x 7 fractions (3,500cGy)	Elderly or significant medical comorbidities
300cGy/fraction x 15 fractions (4,500cGy)	Older, otherwise healthy patients
250cGy/fraction x 20 fractions (5,000cGy)	Younger patients and/or lesions <2cm
200cGy/fraction x 30 fractions (6,000cGy)	Younger patients and/or larger lesions

high- energy and superficial machines. High-energy machines used in radiation oncology target internal malignancies and spare the cutaneous structures.[4] In contrast, superficial machines spare the deeper structures and target the skin, a quality that is ideal for the irradiation and treatment of cutaneous malignancies.

There are few randomized, controlled trials regarding the use of SRT in the treatment of NMSC. However, a number of retrospective analyses and case reports have documented its efficacy with regards to cure, recurrence, and cosmesis. A retrospective analysis performed by Cognetta et al[5] documented the efficacy of SRT in the treatment of more than 1,700 nonaggressive BCCs and SCCs. From 2000 to 2010, a total of 1,715 NMSCs were treated via SRT with a dose fractionation schedule of 700cGy/fraction for a total of five fractions performed three times per week in order to achieve a total dose of 3,500cGy.[5] However, if the lip was affected, a dose fractionation schedule of 500cGy/fraction for a total of seven fractions was occasionally employed.[5] The extent of the tumor was delineated and 5 to 10mm margin or radiation field was determined.[5] Both the histologic type and site of the tumor was recorded and patients were followed for a mean duration of 31.5 months.[5] The cumulative recurrence rates of both BCC and SCC combined at 2 and 5 years were 1.9 percent (95% CI: 1–2.7%) and five percent (95% CI: 3.2–6.7%), respectively.[5] There was a significant difference with regard to both the size of the tumor and sex of the patient. Tumors <2cm in greatest diameter had significantly better recurrence-free rates.[5] Additionally, male patients had worse recurrence rates than their female counterparts. Another retrospective analysis performed by Schulte et al[6] revealed similar results after a total of 1,267 NMSCs were treated with SRT. The majority of patients were treated with a dose fractionation schedule of 500cGy/fraction either three times per week or six days per week with an average total dose of 6,100cGy for BCCs and 6,360cGy for SCCs.[6] Patients were followed for a mean duration of 77 months, and 87.6 percent of patients were followed for at least five years.[6] A recurrence rate of 5.1 percent was found for all NMSCs combined.[6] The most common adverse effects reported include hypopigmentation (72.7%), tel-angiectasias (51.5%), erythema (44.5%), and hyper-pigmentation (23.4%).[6] Additionally, ulceration presenting more than eight weeks following cessation of therapy was reported in 6.3 percent of patients, and 82.5 percent of these ulcerations were able to be treated with conservative measures (i.e., antibiotic ointments or spontaneous resolution).[6] Furthermore, a retrospective analysis by Zagrodnik et al[7] in 2003 documented the results of 175 BCCs treated with SRT. Biopsy-proven diagnoses of BCC were categorized based on histopathology as superficial, nodular, or sclerosing (morpheaform) and treated with varying dose fractionation schedules based on the size of the lesion. The five-year mean recurrence rate for all BCCs included in the study was 15.8 percent.[7] The five-year mean recurrence rates for superficial, nodular, and sclerosing (morpheaform) BCC were 11.8, 2.8, and 27.7 percent, respectively.[7] Approximately 85 percent of all recurrences occurred within the first three years following SRT, and the sclerosing type of BCC was shown to be more resistant to treatment.[7] The results of this trial are concerning as there is a substantial difference in recurrence-free rates in comparison to the aforementioned trials. While BCCs greater than 2cm were treated with higher doses of radiation, the study stratified results based on histologic classification and not tumor size. This distinction is likely the reason for such results, and it is important to consider both the histologic classification and tumor size when utilizing superficial radiation therapy. Another retrospective analysis of 180 SCCs treated with SRT found that increased age and greater size were associated with significantly increased rates of recurrence.[8] Additionally, SCCs of the ear and scalp were associated with significantly lower rates of relapse-free survival in comparison to lesions located on the nose and cheek (79.2% and 69.2% vs. 95.2% and 90.9%).[8] In 2013, Kharofa et al[9] reported the results of a cross-sectional study documenting patient-reported outcomes following SRT for the treatment of NMSCs of the face. The Skin Cancer Index (SCI) was utilized as a measure of quality of life in the 42 patients treated with SRT. The reported SCI scores from this

study were similar to scores obtained from surgical studies and 94 percent of patients reported that they were either satisfied or very satisfied with the cosmetic result.[9] In contrast, a randomized trial comparing the cosmetic outcomes of either surgery or radiotherapy for the treatment of BCC of the face revealed that favorable cosmesis was significantly greater in surgical patients in comparison to those treated with radiotherapy.[10]

As stated, MMS remains the gold standard for the treatment of NMSC. MMS is highly effective, with five-year recurrence rates of approximately one percent for BCC.[1] The recurrence rate for radiation therapy is more, as described above. However, patient-specific and tumor-specific characteristics may preclude the use of MMS making SRT a viable alternative. For example, patient-specific characteristics that would favor SRT include older age at presentation (>70 years old), significant medical comorbidities, anticoagulant/antiplatelet use, or more simply, patient preference. Additionally, tumor-specific characteristics that would favor radiotherapy include the site, size, depth, and stage of the tumor.[3] Sites, such as the ala nasi, nasal tip, nasal bridge, eyelid, medial canthus, and helix, typically require complex closures, often incorporating the use of either grafts or flaps.[3]

Acute reactions, such as erythema and mild discomfort, can be expected during treatment with superficial radiation therapy and systemic side effects are rare.[3] However, patients can expect a healing time of approximately four weeks following the cessation of therapy.[3] Late reactions can be seen anywhere from months to years later and consist of hyper/hypopigmentation, telangiectasias, and atrophy.[3] Mild emollients may be used in the treatment of acute reactions. However, late reactions, including radiation-induced ulcers, require more extensive treatment and are oftentimes irreversible.

As superficial radiation therapy makes its way into more dermatology practices, there will be an increased need for better education regarding the delivery and operation of superficial radiation. Radiation physicists play important roles in both determining the dose of radiation delivered to the patient and the implementation of safety measures for the staff and patient. Additional training in superficial radiation therapy is also essential for all dermatologists who are considering this modality. Such services are typically offered by companies that provide dermatologists with superficial radiation machines. Additional training not only provides dermatologists with the knowledge surrounding the appropriate use of superficial radiation therapy, but ensures that it is both safely and effectively delivered.

In conclusion, SRT is likely a viable alternative for the treatment of BCCs and SCCs in a select group of patients.[11] However, additional studies need to be conducted in order to further delineate its role in the management of both. Consideration should be given to the size, location, and histopathology of the tumor as larger tumors and SCCs located on the scalp and ear have been associated with significantly higher rates of recurrence. Nevertheless, SRT is an additional modality that dermatologists can use to treat skin cancer, especially in the elderly population, that may provide comparable efficacy and cosmesis to more invasive options.

REFERENCES

1. Soyer H, Rigel D, Wurm E. Actinic keratosis, basal cell carcinoma, and squamous cell carcinoma. In: Bolognia J, Jorizzo J, and Schaffer J, eds. *Dermatology*, vol. 2. Philadelphia: WB Sauders; 2012: 1773–1793.
2. Staples MP, Elwood M, Burton RC, et. al. Nonmelanoma skin cancer in Australia: the 2002 national survey and trends since 1985. *Med J Aust.* 2006;184:6–10.
3. David C. Electronic brachytherapy and superficial radiation therapy: will you be adding it to your practice. *Cutis.* 2013;92:E16–E18.
4. Veness M, Richards S. Radiotherapy. In: Bolognia J, Jorizzo J, and Schaffer J, eds. *Dermatology*, vol. 2. Philadelphia: WB Sauders; 2012: 2291–2301.
5. Cognetta A, Howard B, Heaton H, et.al. Superficial X-ray in the treatment of basal and squamous cell carcinoma: a viable option in select patients. *J Am Acad Dermatol.* 2012;67:1237–1241.
6. Schulte KW, Lippold A, Auras C, et. al. Soft X-ray therapy for cutaneous basal cell and squamous cell carcinomas. *J Am Acad Dermatol.* 2005;53:993–1001.
7. Zagrodnik B, Kempf W, Seifert E, et. al. Superficial radiotherapy for patients with basal cell carcinoma. *Cancer.* 2003;98(12):2708–2714.
8. Barysch M, Eggman N, Beyeler M, et. al. Long term recurrence rate of large and difficult to treat cutaneous squamous cell carcinomas after superficial radiotherapy. *Dermatology.* 2012;224:59–65.
9. Kharofa J, Currey A, and Wilson JF. Patient-reported outcomes in patients with nonmelanomatous skin cancers of the face treated with orthovoltage radiation therapy: a cross-sectional study. *Int J Radiation Oncol Biol Phys.* 2013;87(4):636–637.
10. Petit JY, Avril MF, Margulis A, et. al. Evaluation of cosmetic results of a randomized trial comparing surgery and radiotherapy in the treatment of basal cell carcinoma of the face. *Plast Reconstr Surg.* 2000;105:2544–2551.
11. Telfer NR, Colver GB, Morton CA. Guidelines for the management of basal cell carcinoma. *Br J Dermatol.* 2008;159:35–48.